

REMARKS

Reconsideration of this application is respectfully requested. Applicants have amended claim 35 to recite that the Env protein has an amino acid sequence comprising amino acids of HIV-1ELI Env protein. This amendment adds no new matter.

Claims 35-40 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such way as to reasonably convey that applicants had possession of the claimed invention at the time the application was filed. The Examiner contends that the specification does not describe any particular isolate that differs by the claimed number of amino acids (i.e., one, three, five, or seven). In addition, the Examiner contends that the specification does not describe any other HIV-1ELI variants, and that it would be extremely difficult for the skilled artisan to envisage any particular structure for any given variant. Applicants traverse the rejection.

Applicants isolated a novel HIV-1 isolate, HIV-1ELI, and provided its complete nucleotide sequence. (Specification at Fig. 7.) At the time the application was filed, the nucleotide sequence of three HIV-1 viruses was known: HIV-1IIB, HIV-1BRU, and HIV-1ARV-2. (*Id.* at 2, lines 2-6.) The nucleotide sequence of HIV-1ELI differed from the known HIV-1 viruses to a much greater extent than the sequences of the known viruses differed from each other. (*Id.* at 2, lines 30-35.) Thus, applicants discovered that the heterogeneity of HIV-1 was much greater than that which had been previously appreciated. Applicants' claims recite a virus encoding an Env protein that comprises amino acids of HIV-1ELI Env protein that are not present in the three known viruses.

Applicants have amended claim 35 to stress that the claimed virus encodes an Env protein that comprises HIV-1ELI-specific amino acids of Env protein at defined positions. Applicants' specification provides an adequate written description for the claimed invention.

Applicants' specification provides a comparison of the Env amino acid sequence of HIV-1ELI to the Env amino acid sequence of HIV-1BRU and HIV-1ARV-2. (*Id.* at Figs. 3E-1, 3E-2, and 3F-1.) Through this comparison, applicants identified "well conserved stretches" of HIV-1 Env protein. (*Id.* at 23.) Applicants' specification indicates that "[p]roteins containing or consisting of the 'well conserved stretches' are of particular interest" (*Id.* at 23, lines 21-22.) These "well conserved stretches" included aa 37-130, aa 211-289, aa 488-530, and aa 680-700. (*Id.*) As seen in the attached copy of Fig. 3E-1 (Exhibit 1), aa 37-130 contain **seven** amino acids (blue highlighting) in the sequence of HIV-1ELI that are not present in the sequences of HIV-1BRU (orange highlighting) and HIV-1ARV-2 at the same positions: S⁶³, E⁶⁵, A⁶⁸, I⁷¹, I⁸⁷, A⁸⁸, E⁹⁰. As seen in the attached copy of Fig. 3E-1 (Exhibit 1), aa 211-289 contain **five** amino acids (blue highlighting) in the sequence of HIV-1ELI that are not present in the sequences of HIV-1BRU (orange highlighting) and HIV-1ARV-2 at the same positions: A²¹⁵, R²⁴⁴, D²⁴⁵, K²⁴⁷, I²⁸⁶. As seen in the attached copy of Fig. 3E-2 (Exhibit 2), aa 488-530 contain **three** amino acids (blue highlighting) in the sequence of HIV-1ELI that are not present in the sequences of HIV-1BRU (orange highlighting) and HIV-1ARV-2 at the same positions: Q⁵⁰⁹, R⁵¹⁹, E⁵²⁶. As seen in the attached a copy of Fig. 3F-1 (Exhibit 3), aa 680-700 contain **one** amino acid (blue highlighting) in the sequence of HIV-1ELI that is not present in the sequences of HIV-1BRU (orange

highlighting) and HIV-1ARV-2 at the same position: Q⁶⁹⁷. Thus, applicants' specification provides support for an HIV-1ELI Env protein comprising one, three, five, or seven amino acid residues of the amino acid sequence of HIV-1ELI that are not present in the amino acid sequence of HIV-1IIB, HIV-1BRU, or HIV-1ARV-2 at the same positions.

Furthermore, applicants' comparisons in Fig. 3 provide a blueprint of amino acids found in HIV-1ELI that are not present in the sequences of HIV-1BRU and HIV-1ARV-2 at the same positions. Using this blueprint the skilled artisan could generate an enormous genus of HIV-1ELI variants containing HIV-1ELI-specific amino acids. For example, the skilled artisan could generate an HIV-1 virus containing any of the HIV-1ELI-specific amino acids sequence variations shown in Fig. 3, such as a serine at aa 63 and/or an isoleucine at aa 71. Thus, the skilled artisan would understand that applicants had possession of the claimed invention at the time the application was filed. Accordingly, applicants respectfully request withdrawal of the rejection.

Claims 35-40 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly not being supported by an enabling disclosure. The Examiner contends that the disclosure fails to provide a suitable number of working examples and fails to provide any guidance pertaining to those portions of the envelope that can be modified without affecting the normal function of the envelope. Applicants traverse the rejection.

As discussed above, applicants' comparisons in Fig. 3 provide a blueprint of amino acids found in HIV-1ELI that are not present in the sequences of HIV-1BRU and HIV-1ARV-2. Moreover, applicants provided the sequence of the Env protein of an additional HIV-1 isolate that varied greatly from the known HIV-1 strains, HIV-1MAL, in

Fig. 3. Fig. 3 thus provides for an assortment of amino acids that occur at each position in HIV-1 Env protein. In this way, the specification provides guidance as to the portions of the envelope protein that can be modified without affecting normal protein function. The Examiner's assertions to the contrary are in error. Using Fig. 3 as a guide, the skilled artisan could readily generate HIV-1ELI variants, for example, using the well-known technique of site-directed mutagenesis (See Peden et al., Exhibit 4). Moreover, evolution of an HIV-1ELI virus *in vitro* or *in vivo* would be expected to result in HIV-1ELI variants. (See, e.g., Lardner et al. and Stern et al., Exhibits 5 and 6.) Accordingly, applicants respectfully request withdrawal of the rejection.

Applicants respectfully submit that this application is in condition for allowance. In the event that the Examiner disagrees, he is invited to call the undersigned to discuss any outstanding issues remaining in this application in order to expedite prosecution.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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